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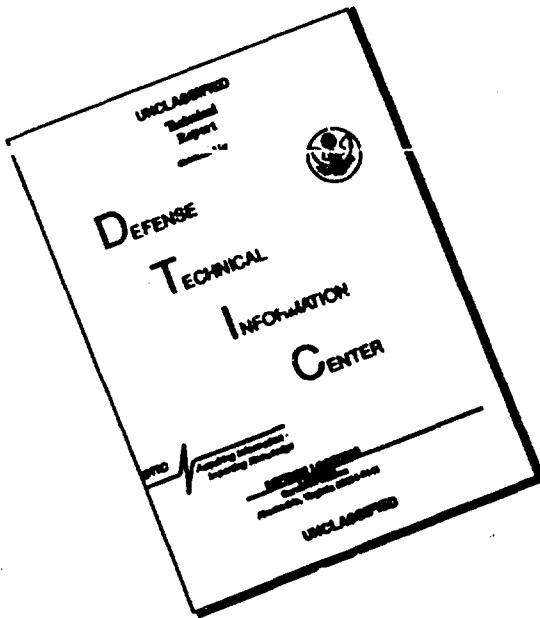
TEMPERATURE RESPONSE IN ANIMALS  
INFECTED WITH BACILLUS ANTHRACIS

Jerry S. Walker  
Frederick Klein  
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FEBRUARY 1967

DEPARTMENT OF THE ARMY  
Fort Detrick  
Frederick, Maryland

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TECHNICAL MANUSCRIPT 360

TEMPERATURE RESPONSE IN ANIMALS INFECTED  
WITH BACILLUS ANTHRACIS

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AGENT DEVELOPMENT AND ENGINEERING LABORATORY

Project 1C522301A059

February 1967

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council.

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TEMPERATURE RESPONSE IN ANIMALS INFECTED  
WITH BACILLUS ANTHRACIS

ABSTRACT

Rats, rabbits, swine, guinea pigs, and monkeys were challenged with anthrax organisms and their temperature responses recorded. These responses were species-specific and varied with the challenging dose. In addition, the rabbit failed to demonstrate a dose response, limiting its usefulness in studying anthrax pathogenesis and immunization.

The temperature response of the mammalian species, including man, to Bacillus anthracis is extremely variable.<sup>1-4</sup> With the exception of two controlled studies,<sup>5,6</sup> most data have been collected from field cases where neither the dose of infecting organism nor the stage of infection was known.

It is the purpose of this report to demonstrate that the variability of temperature response is species-specific and may be dose-dependent in certain species under controlled laboratory conditions.

Fischer 344 rats weighing 0.25 kg, New Zealand white rabbits weighing between 1.8 and 2.7 kg, rhesus monkeys (Macaca mulatta) weighing between 4 and 6 kg, dwarf swine of the Pitman-Moore variety weighing between 10 and 14 kg, and guinea pigs of the Hartley strain weighing 0.25 kg were used in these studies. Spores of the Vlb strain of B. anthracis were used for challenge. Two intraperitoneal (IP) doses,  $10^7$  and  $10^{10}$ , were used to challenge the rabbits and guinea pigs. The swine received  $10^8$  IP, and the monkeys and the rats received  $10^9$  organisms intradermally (ID). In addition, rabbits were challenged with doses of  $10^2$ ,  $10^4$ ,  $10^6$ ,  $10^8$ , and  $10^{10}$  spores in an effort to determine a dose response relationship. Continuous body temperature recordings were made by means of intraperitoneal thermocouples wired to a multiple-point potentiometer, except that the body temperature of swine was taken with a rectal thermometer.

Relative units of time are plotted on the x axes of the graph; that is, the scale runs from 0 to 100, where 0 is the challenge time and 100 is the time to death. A ratio to determine the relative units to actual times in hours was calculated by the following formula:

$$\frac{100}{TD} = \frac{X}{\text{Assay time (hr)}}$$

TD is the time of death in hours, and X is the relative unit to be determined. Assay time is the time that postchallenge temperatures were read. Each point represents the mean of four to six animals at indicated observation times during the course of infection. The resulting curves were plotted by joining the lines to mean values. Temperature variability is expressed as the highest and lowest temperatures recorded at that observation period. Except for the rat and monkey, control temperatures were obtained from the Handbook of Biological Data.

Temperature responses of the different animal species to anthrax infections are summarized in Figure 1. The guinea pig, recognized as a susceptible animal to anthrax infection, appeared to give no response initially to either high or low infecting dose. Temperatures were normal until septicemia onset, then became grossly hypothermic during the terminal stages. The monkey, also susceptible to anthrax infection, showed no febrile reaction of significance as confirmed with base line data, and progressed to hypothermia terminally. Nordberg et al.<sup>6</sup> in work with susceptible rabbits showed a positive correlation between body temperature and an increased number of organisms in the blood. We show two types of temperature reaction, depending on the dose, in the rabbit. The high dosage of organism produced an elevated temperature within the first 10 hours postchallenge that continued until death. Animals given  $10^7$  organisms produced an elevated temperature that peaked at approximately 40 hours and then declined slowly until death. The rabbit also was different from the other species in that no dose response could be demonstrated, as shown in Figure 2.

In general, the temperature response of the resistant species (rats and swine) to anthrax infection was insignificant compared with that of the susceptible animals. Although we were unsuccessful in producing the septicemic disease in swine, the temperature showed a slight elevation at 108 hours postchallenge with a return to normal 24 hours later. The animals survived in all cases. These data confirm reports in the literature<sup>8,9</sup> that a rise in temperature appears characteristic of swine in all acute septicemic field cases. The rat, generally accepted as a resistant animal to *B. anthracis* infection, showed no temperature response to the infecting anthrax organism. Even terminally, a hypothermia was not evident. This was in contrast to work reported by us when rats were challenged with *in vitro* anthrax toxin.<sup>10</sup>

The results of these studies indicate that the temperature response is species-dependent and may vary with the challenging dose. Some species have little if any increase in body temperature during the course of infection and may either succumb to the infection with a normal temperature or become hypothermic. However, in other species the reverse is true. The failure of the rat to respond with a change in body temperature following infection was most likely the result of the low level of organisms and toxin in the blood of this species at death.<sup>11</sup>

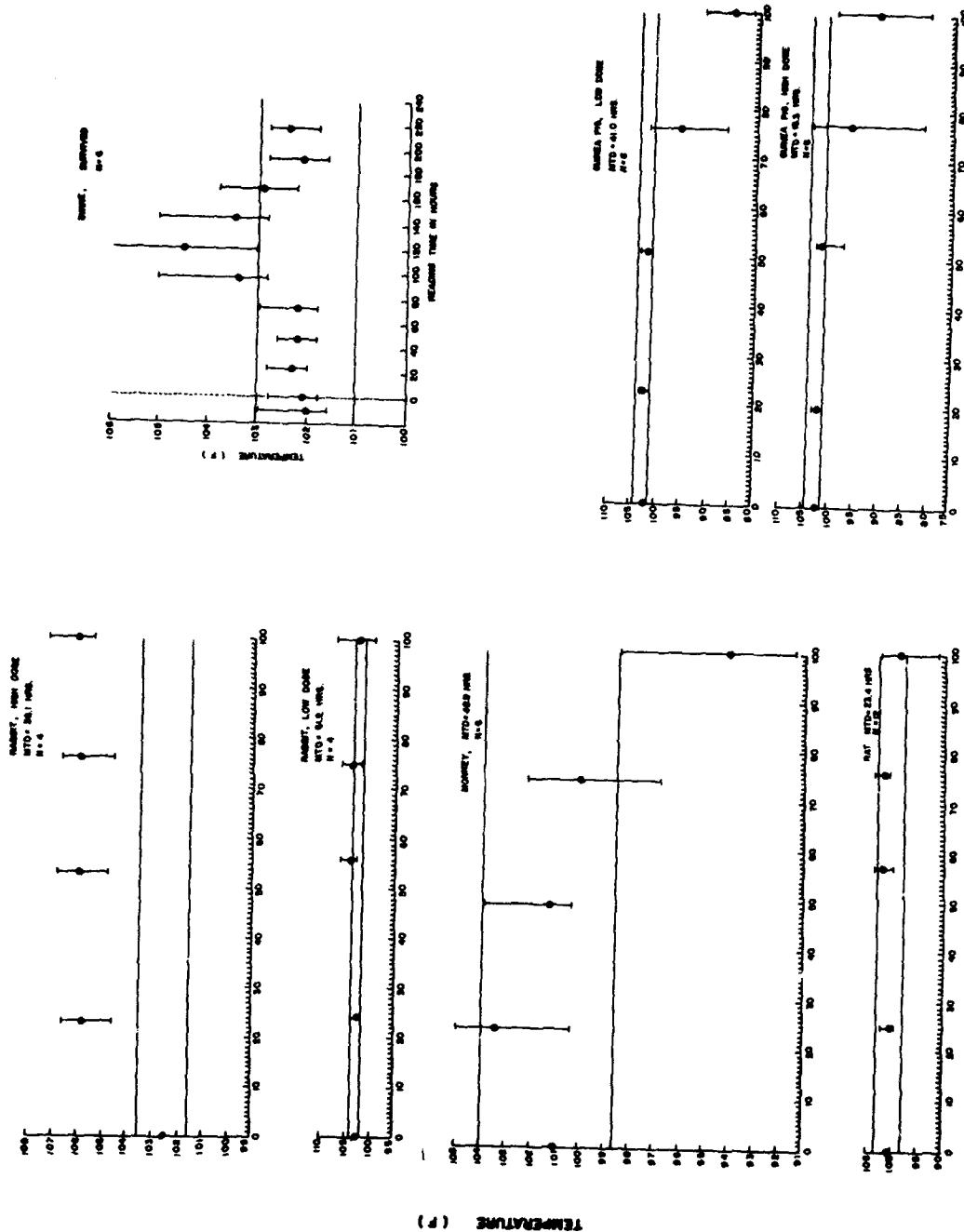


Figure 1. Temperature Responses in *B. anthracis*-Infected Animals.

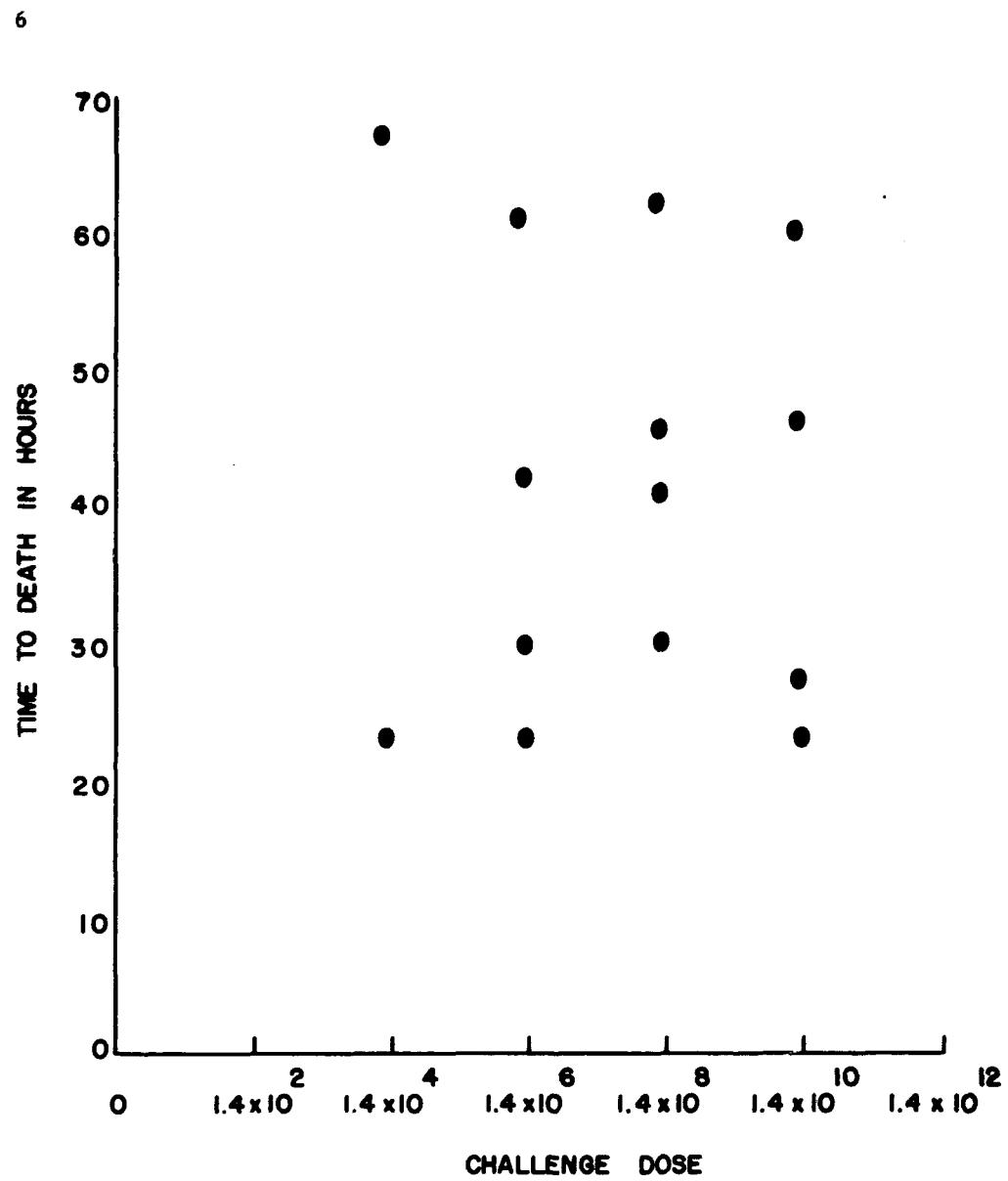


Figure 2. Dose Response of the Rabbit to B. anthracis Spores.

The lack of a dose response in the rabbit was the exception to all other species challenged in our laboratory.<sup>12</sup> This suggests the limited usefulness of the rabbit in studying anthrax pathogenesis or immunization, which would indicate that results obtained with rabbits may be difficult to relate to observations on other species.

The clinical use of temperature to indicate the severity of anthrax infection for prognosis should be discouraged because of the variability among species as reported in the literature and in our findings. The fact that species vary widely in the response suggests that change of temperature is not a primary response to anthrax infection.

LITERATURE CITED

1. Albrink, W.S.; Brooks, S.M.; Biron, R.E.; Kopel, M. 1960. Human inhalation anthrax: A report of three fatal cases. *Amer. J. Pathol.* 36:457-471.
2. Gold, N. 1942. Anthrax: A review of 60 cases with a report on the therapeutic use of sulfonamide compounds. *Arch. Intern. Med.* 70:785-821.
3. Sterne, M. 1959. Anthrax, p. 16-52. In A.W. Stableforth and I.A. Galloway (ed.) *Infectious diseases of animals, diseases due to bacteremia*, Vol. I. Academic Press, Inc., New York.
4. Narasimham, C.V. 1954. An interesting outbreak of anthrax. *Indian Vet. J.* 30:512-514.
5. Smith, H.; Keppie, J. 1962. The terminal phase of anthrax. *Brit. J. Exp. Pathol.* 43:684-686.
6. Nordberg, B.K.; Schmiederow, G.G.; Hansen, N.J. 1961. Pathological investigations into the terminal course of experimental anthrax in the rabbit. *Acta Pathol. Microbiol. Scand.* 53:295-318.
7. National Academy of Sciences. 1956. *Handbook of biological data*. W.S. Spector (ed.) W.B. Saunders Company, Philadelphia, Pa.
8. Bowen, P.D.G. 1953. Anthrax. *Vet. Rec.* 65:140.
9. Ferguson, L.C.; Bohl, E.H. 1958. Anthrax, p. 291-298. In H.W. Dunne (ed.) *Diseases of swine*. Iowa State College Press, Ames, Iowa.
10. Klein, F.; Lincoln, R.E.; Mahlandt, B.G.; Dobbs, J.P.; Walker, J.S. July 1966. Effect of temperature and drug therapy on anthrax intoxication, (Technical Manuscript 310). Process Development Division, U.S. Army Biological Center, Fort Detrick, Frederick, Maryland.
11. Klein, F.; Haines, B.W.; Mahlandt, B.G.; DeArmon, I.A., Jr.; Lincoln, R.E. 1963. Dual nature of resistance mechanisms as revealed by studies on anthrax septicemia. *J. Bacteriol.* 85:1032-1038.
12. Lincoln, R.E.; Walker, J.S.; Klein, F. 1967. Value of field data for extrapolation in anthrax, (Technical Manuscript 349). Process Development Division, Fort Detrick, Frederick, Maryland.

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